UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,124	08/21/2001	James B. Lorens	021044-000210US	8377

20350 7590 09/13/2006

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,124	LORENS ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,14-16,19 and 28-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *31* is/are allowed.

6)☒ Claim(s) *1, 6, 14-16, 19 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 7/11/06, is acknowledged.

2. Claims 1, 6, 14-16, 19 and 28-31 are pending.

3. In view of the amendment filed on 7/11/06, only the following rejection is remained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 6, 14-15, 19 and 28-30 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying a compound that modulates angiogenesis comprising contacting the compound with a cell expressing the ILKAP polypeptide of SEQ ID NO: 2 and determining the angiogenic or loss of angiogenesis phenotypic effect of the compound upon the cell expressing the ILKAP polypeptide, whereby the difference in the angiogenic or loss of angiogenesis effect as compared to the angiogenic or loss of angiogenesis effect in the absence of the compound indicates that the compound modulates angiogenesis. does not reasonably provide **enablement** for a method for identifying a compound that modulates angiogenesis comprising contacting the compound with a cell expressing an ILKAP polypeptide , wherein the ILKAP polypeptide "has at least 90% identity to an amino acid sequence of SEQ ID NO:2", and wherein the ILKAP polypeptide has an anti-angiogenic phenotype in claim 1, wherein the ILKAP polypeptide "has at least 95% identity to an amino acid sequence of SEQ ID NO: 2" in claim 28, wherein the ILKAP polypeptide has at least 90% identity to the amino acid sequence of SEQ ID NO:2 over the entire length in claim 30. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Actions mailed 6/03/04, 1/24/05 and 1/11/06.

At issue is the ILKAP polypeptide that "has at least 90/95% identity to an amino acid sequence of SEQ ID NO: 2" in claims 1, 28 and 30.

Applicant's arguments, filed 7/11/06, have been fully considered, but have not been found convincing.

Applicant points out that *Ex parte Sun et al* the board found claims that recited 80% identity to a reference sequence (a WEE1 protein) were enabled. Applicant contends that the rejections and reasoning applied the WEE1 claims during prosecution are cited against the pending claims, i.e., that alteration of a critical region of the WEE1 protein could affect protein function and therefore, that one of skill in the art would not be able to predict the structure and function of sequence variations of the protein. Applicant submits that the prosecution reasoning in *Sun* was

actually rejected by Board, who ruled that the Examiner **did not** demonstrate that the teachings of the teaching of the application at issue were insufficient for enablement of the claims to 80% identity to a reference sequence. Applicant asserts that in the present Office Action the Examiner has not demonstrated that the evidence presented in *Sun* is somehow more enabling that the evidence relied on by the Applicants in the present case. Applicant concludes that the citation of Sun supports the present Applicants assertion of enablement for claims that recite 90% identity to a reference sequence.

Again, the fact pattern in *Ex part Sun* is not the same the fact pattern presented in the instant case. No critical region was found to affect the anti-angiogenic phenotype of the ILKAP polypeptide so that the skilled artisan would recognize that modification of the critical region would be most likely to have a detrimental effect on the ILKAP activity and avoid such modification in the ILKAP polypeptide. *Ex Parte Sun* doe not address the issue at hands and considered to be irrelevant to the claimed invention.

Applicant further directs the Examiner's attention to *Ex parte Bandman et al.* Applicant submits that in *Bandman*, the board found that claims directed to sequences with 95% identity to a reference sequence were enabled because the supporting specifications provided a single reference sequence and an assay for activity of the encoded protein.

Again, the fact pattern in *Ex part Bandman* is not the same the fact pattern presented in the instant case. The instant claims are not directed to an enzyme as the case in *Bandman, a* malate dehydrogenase. Also, the instant claims are not limited to naturally occurring sequences, (i.e., naturally occurring variants will presumably retain ILKAP activity). Further, the specification on page 44, under example 1 discloses that this clone, designated C1, encoded a partial PP2C-like phosphatase domain. BLAST analysis revealed a single Genbank entry without correlated function, i.e., naturally occurring variants of 90%/95% identity to an amino acid of SEQ ID NO: 2 would not retain ILKAP activity. The specification establishes that structural similarity among PP2C phosphatase is not predictive of functional similarity.

Applicant submits that the Office Action appears to assert that amino acid by amino acid investigation of structure function relationships is required for enablement of claims that recite, e.g., 90% identity to a reference sequence. Applicant submits that both Sun and Bandman reject that analysis and put forth an enablement standard of identification of functional areas in the amino acid sequence of a protein combined with assays to measure activity of the protein.

However, the amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (*In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)). Since no critical region was shown in the specification as critical for the anti-angiogenic phenotypic. It is not clear that reliance on disclosure of sequence information alone would utilize the predicted structural determinations to ascertain functional aspects of the ILKAP protein.

Under the subtitle Evidence in support of Enablement, Applicant submits that the Office Action

did not address the evidence, but rather asserted that the declaration was unsupported and uncorroborated and thus deficient. Applicant submits that based on Dr. Holland's declaration and the supporting references and information in the specification, the skilled in the art would know how to identify ILKAP proteins with 90% identity to the reference sequence that have the recited anti-angiogenic activity.

Contrary to Applicant's assertion, the pervious Office Action dated 1/11/06 addresses the supportive references. The previous Office Action states that neither Leug-Hagesteijn et al nor Applicant's specification establishes that the angiogenesis activity is mediated by modulation of ILK-mediated GSK3β signaling pathway (glycogen synthase kinase 3 β) that one skilled in the art would avoid the phosphatase activity of the ILKAP protein region in screening for the at least 90% identity sequences. The declaration is silent about the relationship between αvβ3 integrin surface expression and such phosphatase activity of the ILKAP protein in angiogenesis. The conserved catalytic domain of cd001434, has not been shown to have an angiogenic activity, even though it has 99.6% alignment with the catalytic domain of SEQ ID NO: 2, i.e., the catalytic domain of SEQ ID NO: 2 is not critical for its angiogenic activity. Therefore, there is no structure and function correlation between the catalytic domain and the angiogenic activity of the ILKAP protein. The claims fail to meet the enablement requirement for the "how to make and use" prongs of the U.S.C 112, 1st paragraph. The instant fact pattern fails to indicate that a representative number of structurally related ILKAP polypeptide is disclosed. The artisan would not know the identity of a reasonable number of representative ILKAP falling within the scope of the instant claim and consequently would not have known how to make them. In order to satisfy 112, first paragraph, the specification has to teach how to make and use the polypeptides of the invention not how to identify the invention.

Applicant again dispute the Office Action's characterization of the knowledge of the function of the ILKAP protein at the time of filing and of two of the citied references: Atwood and Skolnick. Applicant contends that the specification discloses both the identification and functional characterization of the ILKAP protein that occurred before the filing date. Applicant submits that the specification discloses that nucleic acid encoding the ILKAP protein was first disclosed in GenBank and did not include a function for the ILKAP protein, i.e., phosphatase activity and regulation of the ILK protein, in Leung-Hagesteijin et al.

The Examiner agrees with the Applicant with respect that the anti-angiogenic function of the SEQ ID NO:2 did not occurred before the filing date of the instant application. However, the issue here is not the IKAP polypeptide of SEQ ID NO: 2 but the ILKAP polypeptide that "has at least 90/95% identity to an amino acid sequence of SEQ ID NO: 2" in claims 1, 28 and 30 which has an anti-angiogenic phenotype.

Applicant further submits that the skill in the art can carry out at least two assays for ILKAP function: angiogenic assays and phosphatase assays. Applicant submits that there is no requirement in the cited references to empirically determine additional functions for the ILKAP protein or its variants. Applicant further submits that the claimed ILKAP variants that do not have the now-claimed anti-angiogenic phenotype will not be covered by the claims.

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992). The specification fails to provide variants including 90%/95% identity of SEQ ID NO: 2. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed protein in manner reasonably correlated with the scope of the claims broadly including any number of variants of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement. The specification does not provide for sufficient enablement for variants including 90%/95% of SEQ ID NO: 2 other than the one defined by SEQ ID NO: 2; which in turn, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Under Undue Experimentation, Applicant argues that asserts that molecular biologists routinely screen large numbers of candidate molecules for a nucleic acid or protein associated with a phenotype of interest. Applicant submits that assay to identify ILKAP polypeptides that have an anti-angiogenic phenotype and that are 90% identical to SEQ ID NO: 2 are disclosed in the specification can be routinely performed by those of skill, even in "astronomically" large numbers.

While experimental testing techniques assays are available, it is not routine in the art to use such methods when the expectation of success is unpredictable based on the instant disclosure. Thus, it would require an undue amount of experimentation of one skilled in the art to practice the invention as broadly claimed.

Applicant contends that it is well known that using flow cytometry those of skill can assay 5000 cells per second. Applicant contends that the disclosed flow cytometry assays can easily be used to screen large number of candidates for proteins with 90% identity to SEQ ID NO:2 and the recited anti-angiogenic function. Applicant contends that flow cytometry assays are routinely performed by molecular biologists and daily screens of several thousands to millions of potential molecules are also routinely performed by molecular biologists. Applicant concludes that any experimentation required to identify an allegedly rare functional ILKAP polypeptide with 90% identity to SEQ ID NO:2 would not be undue.

However, while the Examiner agree with applicant that the flow cytometry technique is will known, however, the 90% sequence homology to SEQ ID NO: 2 is not know. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g., such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in theses positions. There is no adequate guidance as the nature of active variants that may be constructed, but is merely an invitation to the artisan to sue the current invention as a starting point for further experimentation.

6. Claim 16 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. Claim 31 is allowable.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 28, 2006

Maher Haddad

Maher Haddad, Ph.D.
Primary Examiner
Technology Center 1600